REMARKS

The Non-Final Action/Restriction Requirement mailed January 13, 2006 has been received and carefully considered. Reconsideration of the objections and restrictions set forth therein is respectfully requested in view of the foregoing amendments and the following remarks.

Claims 1-14, 17, 19-25 are pending. Claims 15-16 have been withdrawn by the Examiner. Applicant(s) submit proposed amendments to claims 17, 18 and 21 herewith for the Examiner's consideration and entry if deemed necessary. In the proposed amendments, claim 18 has been cancelled without prejudice. No new matter has been added by the amendments.

I. SEQUENCE COMPLIANCE

Applicant(s) encloses herewith both a substitute computer readable form and substitute paper copy of a Substitute Sequence Listing for insertion in the present application following from page 61. This Substitute Sequence Listing is intended to replace the previous Sequence Listing submitted on March 25, 2005. Applicant(s) hereby states that the information recorded in computer readable form is identical to the written sequence listing.

This substitute Sequence Listing has been revised to include and identify the sequence listing shown in claim 25, which was unintentionally omitted from the Listing due to typographical error. The amino acid sequence of claim 25 is described in the specification, e.g., on page 42, lines 13-16. In addition, the specification has been amended (namely on page 42, line 15 in the Substitute Specification filed on July 14, 2004, as shown above) to include the appropriate sequence identifier "SEQ. ID. NO: 5".

No new matter has been added by the amendments.

Applicant(s) believes compliance with the Sequence rules have now been met and respectfully requests withdrawal of the objection.

II. ELECTION/RESTRICTIONS

In response to the Restriction Requirement, Applicant(s) herewith elects, with strong traverse, claims 1-14 of Group I directed to a replication competent recombinant adenovirus.

Claims 1-14 are directed to a replication competent recombinant virus capable to replicate in target cells and to lyse these cells, which, e.g., have a functional p53 deficiency. The virus comprises, e.g., a factor, restoring the p53 deficiency in the target cells. Thus, upon infection of the target cells that are functionally p53 deficient, p53 functionality is restored. The virus replicates and the cells lyse and die.

Claims 17-20 are directed to a method to lyse the target cells by infection with this virus. This concept (the effect of the virus in the appropriate target cells) is clearly linked to the concept of claims 1-14 (which claim the virus itself). Claims 21-25 are directed to a similar method as claims 17-20, wherein now the target cells are within a subject body.

With respect to WO95/12660, it is respectfully pointed out that this reference is not relevant to the present invention. In WO95/12660, only replication *deficient* recombinant adenoviruses are described. E.g., page 7, lines 9-23 describe that the viruses are NOT capable of replicating! Indeed, it is clearly shown that the viral genome in fact lacks E1A and E1B, rendering such a virus replication defective. In fact, according to WO95/12660, it is intended to treat p53-linked cancers by treatment with adenoviral p53-gene constructs **without** replication of the virus in the cancer cells. Further proliferation of cancer is thus caused to be prevented by invoking tumor growth *inhibition*, NOT by lysing/killing the cells. *See* e.g., page 33, lines 6-16 of WO95/12660.

In stark contrast, in the present invention a replication *competent* virus is provided, i.e., resulting in lysing (i.e., killing) of the target cells. Advantageously, as a result, instead

of tumor growth inhibition (as obtained in WO95/12660), an effective killing of the target cells is indeed achieved, which is wholly not disclosed, taught, suggested or envisaged by WO95/12660.

Note that throughout WO95/12660, the envisaged adenovirus is clearly intended and stated to be replication defective. *See* e.g., page 11, lines 1-4: "[I]t should be pointed out that because the adenovirus vector employed is replication defective, it will not be capable of replicating in the cells, such as cancer cells, that are ultimately infected" and also on page 48, lines 28-30: "[I]n any event, since the adenovirus employed will be replication incompetent, no deleterious effect of the virus itself on subject health is anticipated."

In summary, WO95/12660 teaches a replication **defective** adenovirus comprising p53 to ***inhibit*** (malignant) cell growth, whereas the present invention teaches a replication **competent** adenovirus conferring p53 functionality to effectively ***kill*** the cells. Accordingly, the Applicant(s) respectfully asserts that the cited WO95/12660 is inapplicable and irrelevant to the subject matter of the present invention, such that it cannot be held against the existence of a single general inventive concept between Groups I, II and III.

Applicant(s) indeed notes the Examiner's acknowledgement of the existence of a special technical feature which links the inventions of Groups I, II and III. In light of at least the above explanation and arguments, it is respectfully asserted that the inventions stated by the Examiner of groups I, II and III are similar enough such that a search for elements associated with a replication competent recombinant virus capable of replicating and lysing target cells would necessarily overlap a search for methods of lysing target cells/treatment of a subject body with such replication competent virus. The Applicant(s) believe this would

not cause an undue burden in examination. Accordingly, Applicant(s) respectfully request reconsideration and withdrawal of the Restriction Requirement.

In the event these arguments are not deemed sufficiently persuasive, **please enter the proposed amendments to claims 17, 18 and 21.** Namely, the Applicant(s) has further amended claim 17 to refer to the recombinant virus of claim 1, in an effort to further emphasize linkage of a single inventive concept. In addition, Applicant has amended claim 21 to make reference to the virus of claim 1, to further emphasize linkage of the inventive concepts. In light of these amendments, Applicant(s) respectfully request withdrawal of the Restriction Requirement and examination of Groups I, II and III collectively in this application.

CONCLUSION

It is believed that no additional fees or charges are currently due. However, in the event that any additional fees or charges are required at this time in connection with the application, they may be charged to applicant's representatives Deposit Account No. 50-1433.

Respectfully submitted,
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